



Peripheral artery disease independently associated with significantly higher risk for COVID-19 mortality: Evidence based on adjusted effect estimates

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Abstract

Objective: To investigate the influence of peripheral artery disease (PAD) on the risk of mortality among coronavirus disease 2019 (COVID-19) patients based on adjusted effect estimates.

Methods: Systematic searches were performed through electronic databases. A random-effect model was applied to calculate the pooled effect and corresponding 95% confidence interval (CI). Inconsistency index (I^2) was used to evaluate the heterogeneity across studies. Sensitivity analysis, subgroup analysis, and Begg's test were all implemented.

Results: On the basis of 16 eligible studies with 142,832 COVID-19 patients, the meta-analysis showed that PAD significantly increased the risk for mortality among COVID-19 patients (pooled effect = 1.29, 95% CI: 1.10–1.51). The significant association was also observed in the subgroup analysis stratified by hospitalized patients, mean age ≥ 60 years, Europe and North America. Sensitivity analysis verified the robustness of our findings. Begg's test ($P = 0.15$) showed there was no potential publication bias.

Conclusions: COVID-19 patients with PAD may have a greater risk of mortality. Clinicians and nursing staff are supposed to identify and monitor these high-risk patients in a timely manner and provide appropriate clinical treatment for them.

Keywords

Peripheral artery disease, COVID-19, mortality, meta-analysis

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Recently, Zuin et al.¹ have published a meta-analysis in this journal and indicated that peripheral artery disease (PAD) was significantly associated with a two-fold greater risk of death of coronavirus disease 2019 (COVID-19) patients. This is an interesting study. However, the conclusion was summarized on the basis of unadjusted effect estimates without controlling potential confounders. To our knowledge, several covariates such as age, sex, and comorbidities markedly affect the clinical outcome of COVID-19,^{2,3} which may modulate the relationship between PAD and COVID-19 mortality. For instance, Li et al.⁴ performed a univariate analysis and revealed that PAD was correlated with significant higher mortality risk of COVID-19 while the significant association was not observed in the

multivariate analysis. Besides, the adjusted correlation reported across individual studies have not been consistent.^{5–8}

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Table 1. Basic characteristics of the included studies.

Author	Country	Setting	Sample size	Age	Male (%)	Adjusted effect estimate (95%CI)
Tanboğa IH	Turkey	Hospitalized	60,980	49 (36–63)	53.0	0.85 (0.71–1.01)
Gonzalez-fajardo JA	Spain	Hospitalized	106	65.66 ± 15.49	67.9	7.476 (1.634–34.202)
Girardin JL	USA	Hospitalized	4210	61.89 ± 18.82	58.1	1.33 (1.05–1.69)
Li W	China	Hospitalized	1125	58.3 ± 15.1	49.9	0.76 (0.18–3.25)
Caro-codón J	Spain	Hospitalized	918	63.2 ± 15.5	60.1	1.84 (1.08–3.12)
Scoccia A	Italy	Hospitalized	1625	69 (58–77)	67.2	2.03 (1.19–3.67)
Cummins L	UK	Hospitalized	1,781	59.2	55.2	1.37 (0.74–2.52)
Budweiser S	Germany	Hospitalized	526	73 (57–82)	53.4	1.42 (0.52–4.31)
Cai M	USA	All patients	49,238	63.3 (49.8–73.1)	88.5	1.09 (0.92–1.29)
Rieder M	Germany	All patients	1,433	71.30 ± 13.29	60.2	0.80 (0.48–1.32)
Marquès M	Spain	Hospitalized	2,112	66.55 ± 17.74	57.1	1.33 (0.81–2.14)
Kikuchi K	Japan	Hospitalized	1,010	80	70.2	1.49 (1.05–2.10)
Poli D	Italy	Hospitalized	1,091	71 (59–82)	59.9	4.90 (1.60–15.10)
Palaïodimos L	USA	Hospitalized	8,833	62 (49–74)	59.3	0.939 (0.676–1.305)
Smolderen KG	USA	Hospitalized	3,830	63.1 ± 18.4	49.5	1.45 (1.11–1.88)
Piskač živković N	Croatia	Hospitalized	4,014	74 (64–82)	56.2	1.40 (1.08–1.80)

Notes: CI, confidence interval.

Therefore, it is an urgent need to perform an updated meta-analysis based on risk factors-adjusted effects to clarify this association.

A systematical literature retrieval was carried out among several electronic databases including Web of Science, Scopus, PubMed, Wiley, Springer and Elsevier Science-Direct to recognize all eligible studies published as of 7 May 2022 using the following keywords: “COVID-19,” “SARS-CoV-2,” “peripheral artery disease,” and “mortality.” Only peer-reviewed articles published in English investigating the risk factor-adjusted association between PAD and COVID-19 mortality were enrolled. Heterogeneity was measured by inconsistency index (I^2). A random-effects model was applied to calculate the pooled effect and 95% confidence interval (CI). Sensitivity analysis was performed to check the stability of our study. Begg’s test was conducted to evaluate the publication bias. Statistical analyses were conducted on R software (Version 4.1.2). All reported p -values are two-tailed and $p \leq 0.05$ indicated statistical significance.

Totally, 16 eligible studies including 142,832 cases were enrolled in this meta-analysis (Table 1). This meta-analysis indicated that PAD was significantly associated with a higher risk for mortality in COVID-19 patients (pooled effect = 1.29, 95% CI: 1.10–1.51; Figure 1(a)). When the participants were only limited to hospitalized COVID-19 patients, PAD was still significantly associated with a higher risk for COVID-19 mortality (pooled effect = 1.37, 95% CI: 1.14–1.64). The significant association was also observed in studies with mean age ≥ 60 years (pooled effect = 1.35, 95% CI: 1.13–1.60), Europe (pooled effect = 1.19, 95% CI: 1.01–1.41) and North America (pooled effect = 1.55, 95% CI: 1.18–2.03). Sensitivity analysis verified the stability and robustness of our results (Figure 1(b)).

Begg’s test showed that there was no publication bias ($p = 0.15$, Figure 1(c)).

In conclusion, this current meta-analysis on the basis of adjusted effect sizes indicated that PAD was independently associated with a significantly higher risk for COVID-19 mortality. We hope our present findings will contribute to more accurate elaboration and substantiation of the data reported by Zuin et al.

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Author contributions

Haiyan Yang and Yadong Wang conceptualized the study. Jiahao Ren, and Yuqing Hao performed literature search and data extraction. Jiahao Ren and Lan Nan analyzed the data. Jiahao Ren wrote and reviewed the manuscript. All the authors approved the final manuscript.

Declaration of conflicting interests

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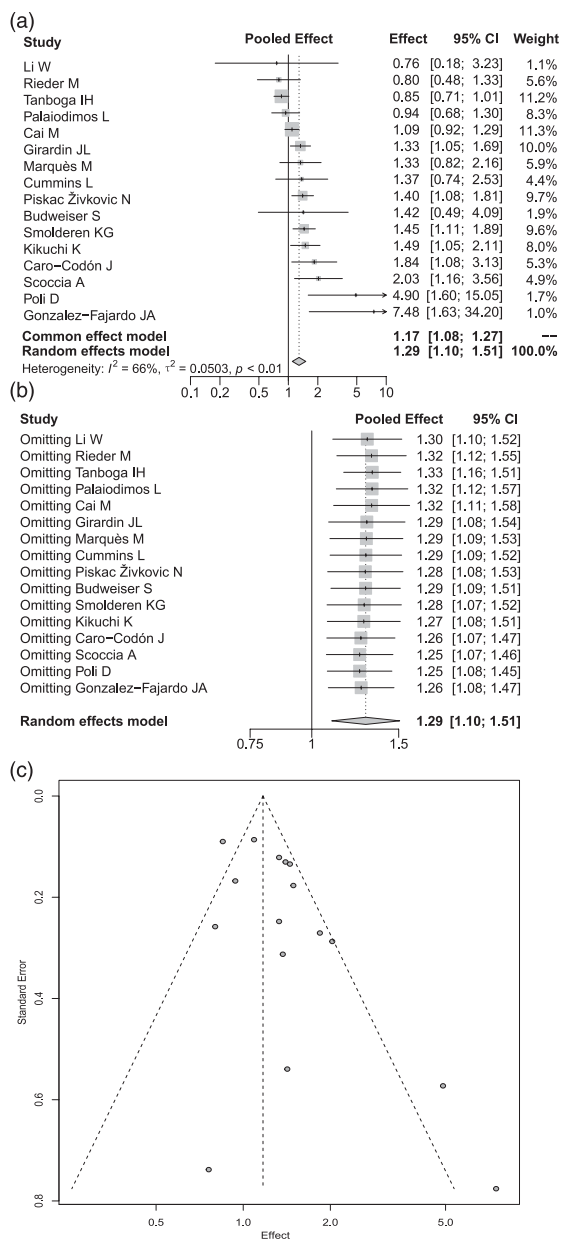


Figure 1. (A) Forest plot indicated the significant association between peripheral artery disease (PAD) and higher risk for mortality of coronavirus disease 2019 (COVID-19) patients; (B) Sensitivity analysis exhibited the stability of the overall result; (C) Funnel plot showed no potential publication bias.

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Data availability

All data relevant to this study are included in this article or uploaded as supplementary file.

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